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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/089,450 | 03/29/2002 | Gilbert Gorr | STURK 0003 | 9421 |

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| EXAMINER |
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KUBELIK, ANNE R

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| ART UNIT | PAPER NUMBER |
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1638

DATE MAILED: 06/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|-----------------|--------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/089,450 | GORR ET AL. | |
| | Examiner | Art Unit | |
| | Anne R. Kubelik | 1638 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6, 17 and 18 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 17 and 18 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

RD

DETAILED ACTION

1. Claims 1-6 and 17-18 are pending.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
3. The objection to claims 4, 6, 8-10 and 14-16 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim is withdrawn in light of Applicant's amendment to the claims.
4. The rejection of claims 1-2, 4-5 and 8-13 under 35 U.S.C. 102(b) as being anticipated by Houba-Hérin et al (1999, Plant J. 17:615-626) is withdrawn in light of Applicant's arguments that Houba-Hérin et al only uses protoplasts.
5. The rejection of claims 1-16 under 35 U.S.C. 103(a) as being unpatentable over Houba-Hérin et al (1999, Plant J. 17:615-626) in view of Nasu et al (1997, J. Ferm. Bioengin. 84:519-523) is withdrawn in light of Applicant's arguments.

Claim Rejections - 35 USC § 112

6. Claims 1-6 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for the production of proteins in *Physcomitrella patens*, does not reasonably provide enablement for a method for the production of proteins in other mosses or in liverworts. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The rejection is repeated for the reasons of record as

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set forth in the Office action mailed 4 October 2005, as applied to claims 1-16. Applicant's arguments filed 4 March 2005 have been fully considered but they are not persuasive.

Applicant urges that Zeidler et al and Nasu et al teach transformation of the moss *Ceratodon purpureus* and the liverwort *Marchantia polymorpha*, respectively (response pg 8-10 and 14).

This is not found persuasive because neither the specification nor the prior art teach methods of transformation for any *Funaria*, *Sphagnum* or *Sphaerocarpos* species or for any *Physcomitrella*, *Ceratodon* or *Marchantia* species other than *P. patens*, *C. purpureus* or *M. polymorpha*, much less any protonema-forming moss or liverwort. There are, for example, at least 6 *Marchantia* species other than *M. polymorpha* (*M. calcarata*, *M. emarginata*, *M. foliacea*, *M. inflexa*, *M. paleacea*, and *M. subintegra*).

Furthermore, the specification must teach how to carry out the invention, and it does not teach how to transform *C. purpureus* or *M. polymorpha*. See *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

Applicant urges that many species of mosses and liverworts were well-known, characterized and studied, citing Reski and Rudolph et al, that the specification teaches transformation of *P. patens* as a working example and that Reutter et al and Houba-Herlin et al teach use of *P. patens* for enzyme and cytokine production (response pg 11-12).

This is not found persuasive because transformation is not taught for species within the full scope of the claims. The rejection is a scope of enablement rejection and stated that the invention was enabled for *P. patens*.

Applicant urges that each of Reski and Nasu teach that these organisms are simple and predictable with well-developed state of the art, citing Houba-Herin, Reuter, Zeidler, Nasu, Rasmussen and Muhlbach (response pg 12-13).

This is not found persuasive because none of Reski, Nasu, Houba-Herin, Reuter, Zeidler, Nasu, Rasmussen or Muhlbach teach transformation for species within the full scope of the claims.

Applicant urges that those of ordinary skill in the art of transforming plants to express selected proteins are highly trained with advanced degrees (response pg 13-14).

This is not found persuasive because the specification must teach how to make and use the invention as claimed and does not.

Applicant urges that the crux of the invention is obtaining heterologous proteins from culture medium without disrupting the producing tissues or cells and some experimentation may be required to do this in protonema species other than *P. patens*, *C. purpureus* or *M. polymorpha*; one of ordinary skill in the art would know how to transform protoplasts of those species, but transformation is not the crux of the invention (response pg 14-15).

This is not found persuasive. Methods of transformation are required to practice the invention for protonema tissue to be able to make heterologous proteinaceous substances. Undue trial and error experimentation would be required to develop a transformation method for the protonema forming mosses and liverworts as encompassed by the claims, if transformation is even possible.

Applicant urges that the claims are not overly broad because they are limited to a method using protonema tissue (response pg 15).

This is not found persuasive because transformation is not taught for protonema forming species within the full scope of the claims.

7. Claims 4-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is different from the rejection set forth in the Office action mailed 4 October 2005.

Claim 4 is indefinite in their recitation of “tissue is selected from the group consisting of mosses and liverworts” as mosses and liverworts are not tissues but types of organisms. Thus, this is an improper Markush group.

Claim Rejections - 35 USC § 103

8. Claims 1-5 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Houba-Hérin et al (1999, Plant J. 17:615-626) in view of Reutter et al (1996, Plant Tiss. Cult. Biotechnol. 2:142-147). The rejection is modified from the rejection set forth in the Office action mailed 4 October 2005, as applied to claims 1-5 and 7-13. Applicant’s arguments filed 4 March 2005 have been fully considered but they are not persuasive.

The claims are drawn to a method of isolating a heterologous protein from culture medium in which in *P. patens* protonema were grown.

Houba-Hérin et al teach a method of producing a biologically active heterologous protein in the moss *P. patens*. The protein was a maize cytokinin oxidase and the activity of this enzyme was detected in the culture medium in which protoplasts were grown (pg 619, right column,

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paragraph 1). Houba-Hérin et al do not disclose isolation of the enzyme in culture media in which protonema were grown.

Reutter et al teach growth of *P. patens* protonema transformed with a nucleic acid encoding a heterologous protein (pg 143, paragraph 2-3) and that these protonema produced large amounts of the heterologous protein (Fig. 3). Reutter et al also teach that *P. patens* can be grown on inorganic medium (pg 142, paragraph 4).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing a heterologous protein in *P. patens* as taught by Houba-Hérin et al, to grow the protoplasts to the protonema stage as described in Reutter et al. One of ordinary skill in the art would have been motivated to do so because Houba-Hérin et al suggest producing the enzyme in a plant system in order to get the proper processing of the enzyme (pg 621, right column, paragraph 2).

Applicant urges that Houba-Hérin et al teaches culturing protoplasts, not protonema (response pg 18-19).

This is not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicant urges that Reutter et al is silent with respect to isolating GUS without disrupting cells or tissues (response pg 19).

This is not found persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the

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rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

9. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Houba-Hérin et al in view of Reutter et al as applied to claims 1-2, 4-5 and 17-18 above, and further in view of Nasu et al (1997, J. Ferm. Bioengin. 84:519-523)

The claims are drawn to a method of isolating a heterologous protein from culture medium in which in liverwort protonema were grown.

The teachings of Houba-Hérin et al in view of Reutter et al are discussed above. Houba-Hérin et al in view of Reutter et al do not disclose a method of isolating a heterologous protein from culture medium in which in protonema were grown, wherein the protonema were from a liverwort.

Nasu et al teach transformation of *Marchantia polymorpha* (pg 520, left column, paragraphs 1-2). *Marchantia polymorpha* is a photoauxotroph, and thus its growth does not require sugars, vitamins, or phytohormones.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of producing a heterologous protein in protonema tissue as taught by Houba-Hérin et al in view of Reutter et al, to use liverwort protonema as described in Nasu et al. One of ordinary skill in the art would have been motivated to do so because substitution of one bryophyte for another is an obvious optimization of design parameters.

Conclusion

10. No claim is allowed.

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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Anne R. Kubelik, Ph.D.
May 26, 2005



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PRIMARY EXAMINER**